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Registration Decision RD2012-31

Fluxapyroxad

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Registration Decision for Fluxapyroxad

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Xemium Technical Fungicide and the end-use products BAS 700 01F Fungicide containing fluxapyroxad, BAS 700 02 F Fungicide Seed Treatment containing fluxapyroxad, BAS 700 03 F Fungicide Seed Treatment containing fluxapyroxad, BAS 700 04 F Fungicide Seed Treatment containing fluxapyroxad, BAS 703 01 F Fungicide containing fluxapyroxad and pyraclostrobin and BAS 703 02 F Fungicide containing fluxapyroxad and pyraclostrobin to control or suppress various fungal diseases in numerous crops.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2012-09, *Fluxapyroxad*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for fluxapyroxad and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2012-09, *Fluxapyroxad*. This decision is consistent with the proposed registration decision stated in PRD2012-09, *Fluxapyroxad*.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-09, *Fluxapyroxad* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is Fluxapyroxad?

Fluxapyroxad is the active ingredient in the following fungicide end-use products, BAS 700 01F Fungicide, BAS 700 04F Fungicide, BAS 703 01F Fungicide, BAS 703 02F Fungicide, BAS 700 02F Fungicide Seed Treatment and BAS 700 03F Fungicide Seed Treatment. Fluxapyroxad belongs to the Group 7 class of fungicides, the succinate-dehydrogenase inhibitor (SDHI). It inhibits succinate-dehydrogenase in complex II of fungal respiration. Fluxapyroxad inhibits spore germination, germ tube elongation, mycelial growth, and sporulation with preventative and curative properties.

Health Considerations

Can Approved Uses of Fluxapyroxad Affect Human Health?

Fluxapyroxad is unlikely to affect your health when used according to label directions.

Potential exposure to fluxapyroxad may occur through the diet (food and water) or when handling and applying the products. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the technical grade active ingredient fluxapyroxad was of low acute toxicity by the oral, dermal and inhalation routes of exposure. Fluxapyroxad was non-irritating to the eyes and minimally irritating to the skin, and did not elicit an allergic skin reaction.

The acute toxicity of the end-use product BAS 700 01 F Fungicide containing fluxapyroxad was low via the oral, dermal and inhalation routes of exposure. It was slightly irritating to the skin and did not cause an allergic skin reaction. BAS 700 01 F Fungicide was severely irritating to the eyes; consequently, the hazard signal words "DANGER – EYE IRRITANT" are required on the label.

The acute toxicity of the end-use product BAS 700 02 F Fungicide Seed Treatment containing fluxapyroxad was low via the oral, dermal and inhalation routes of exposure. BAS 700 02 F Fungicide Seed Treatment contains a red pigment that prevented an optimal evaluation of skin and eye irritation as well as skin sensitization. BAS 700 03 F Fungicide Seed Treatment was non-irritating to the skin and eye and did not cause an allergic skin reaction.

The acute toxicity of the end-use product BAS 700 04 F Fungicide containing fluxapyroxad was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the skin, non-irritating to eyes and did not cause an allergic skin reaction.

The acute toxicity of the end-use product BAS 703 01 F Fungicide containing fluxapyroxad and pyraclostrobin was low via the dermal route of exposure. BAS 703 01 F Fungicide was highly toxic orally and slightly toxic via the inhalation route of exposure. It was minimally irritating to the eyes and mildly irritating to the skin. It did not cause an allergic skin reaction. Consequently, the hazard signal words "DANGER – POISON - SKIN IRRITANT" are required on the label.

The acute toxicity of the end-use product BAS 703 02 F Fungicide Seed Treatment containing fluxapyroxad and pyraclostrobin was low via dermal and inhalation routes of exposure. It was moderately toxic via the oral route of exposure. It was minimally irritating to the eyes and did not cause an allergic skin reaction. BAS 703 02 F Fungicide was mildly irritating to the skin; consequently, the hazard signal words "WARNING – POISON – SKIN IRRITANT" are required on the label.

In animals given daily doses of fluxapyroxad over long periods of time decreases in body weight and body weight gain and changes to the liver and thyroid were observed. Fluxapyroxad did not damage genetic material, however, it caused liver and thyroid tumours in rats above certain dose levels. There was no indication that fluxapyroxad caused damage to the nervous system or immune system. Fluxapyroxad did not cause birth defects in the developing young, or effects on the reproductive system. When fluxapyroxad was given to pregnant or nursing animals, effects on the developing foetus (paw hyperflexion) and juvenile animal (body weight) were observed at doses that were toxic to the mother, indicating that the young were not more sensitive to fluxapyroxad than the adult animal. The risk assessment protects against the effects of fluxapyroxad by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants less than one year old, the subpopulation which would ingest the most fluxapyroxad relative to body weight, are expected to be exposed to less than 40% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluxapyroxad is not of concern for all population subgroups. There were no cancer risks of concern for fluxapyroxad.

Acute dietary (food and water) estimates for the general population and all population subgroups were less than 5% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was infants less than one year old.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using fluxapyroxad on sugar beets, potatoes, soybeans, peas, beans, tomatoes, peppers (bell and non-bell), apples, pears, cherries, peaches, plums, corn (field and sweet), wheat, sorghum, rice, barley, canola, sunflowers, cottonseed and peanuts were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Proposed Registration Decision Document.

The use of active ingredient pyraclostrobin in a coformulation with fluxapyroxad on oilseeds, legumes, cereals and grasses is acceptable. The uses were previously assessed and are considered to be not of health concern.

Risks in Residential and Other Non-Occupational Environments

Residential and non-occupational risks are not of concern when BAS 700 01 F Fungicide and BAS 700 04 F Fungicide are used according to the proposed label directions.

Adults, youth and toddlers may be exposed to fluxapyroxad during pick-your-own harvesting activities. In addition, adults and youth may be exposed to fluxapyroxad during harvesting of fruit from trees in residential settings. Based on the expected short- to intermediate-term duration of these activities, risk to the general population is not of concern. There were no cancer risks of concern.

Occupational Risks From Handling BAS 700 01 F Fungicide, BAS 700 04 F Fungicide, BAS 703 01 F Fungicide, BAS 703 02 F Fungicide, BAS 700 02 F Fungicide Seed Treatment, and BAS 700 03 F Fungicide Seed Treatment

Occupational risks are not of concern when BAS 700 01 F Fungicide, BAS 700 04 F Fungicide, BAS 703 01 F Fungicide, BAS 703 02 F Fungicide, BAS 700 02 F Fungicide Seed Treatment, and BAS 700 03 F Fungicide Seed Treatment are used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply BAS 700 01 F Fungicide, BAS 700 04 F Fungicide, BAS 703 01 F Fungicide or BAS 703 02 F Fungicide as well as field workers re-entering freshly treated fields can come in direct contact with fluxapyroxad residues on the skin. Therefore, the labels specify that anyone mixing/loading and applying BAS 700 01 F Fungicide or BAS 700 04 F Fungicide must wear long-sleeved shirt, long pants, chemical-resistant gloves and goggles or a face shield. BAS 703 01 F Fungicide and BAS 703 02 F Fungicide are co-formulations with pyraclostrobin. Additional personal protective equipment

(PPE) are required for mixer/loader/applicators using these two products: coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves and goggles or a face shield. Custom applicators treating crops with BAS 703 01 F Fungicide and BAS 703 02 F Fungicide must also use groundboom equipment with an enclosed cab. The labels of BAS 700 01 F Fungicide, BAS 700 04 F Fungicide, BAS 703 01 F Fungicide and BAS 703 02 F Fungicide also require that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals from exposure to fluxapyroxad are not a concern. There were no cancer risks of concern.

Workers treating soybean seeds with BAS 700 02 F Fungicide Seed Treatment or BAS 700 03 F Fungicide Seed Treatment in commercial seed treatment facilities and workers planting treated soybean seed can come into direct contact with fluxapyroxad residues on the skin or through inhalation of dust and mists. Therefore, the labels specify that workers treating and handling treated seed must wear the following PPE. Treaters and cleaners must wear coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks. Baggers, bag sewers, stackers, planters and others must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes, and socks. Closed transfer is required for the commercial seed treatment of soybean seed. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals is not a concern. There were no cancer risks of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Fluxapyroxad Is Introduced Into the Environment?

Fluxapyroxad enters the environment when used as a fungicide on foliage of dry beans, pome fruits, stone fruits and a variety of agricultural crops and when used as seed treatment. Based on its low volatility, fluxapyroxad residues are not expected in the air. Once fluxapyroxad enters the terestrial environment, it is expected to adsorb to soil. Under aerobic conditions, transformation of fluxapyroxad is slow with the primary route of transformation by microbial action. Neither hydrolysis nor phototransformation plays important role in the transformation of fluxapyroxad in terrestrial environments. Fluxapyroxad will transform to two major transformation products M700F001 and M700F002. Fluxapyroxad is moderately persistent to persistent in aerobic soils while the transformation product M700F001 is not persistent in aerobic soils, M700F002 is moderately persistent.

Available data and modelling results suggest fluxapyroxad has potential to leach. The transformation products (M700F001 and M700F002) have very high mobility; hence also have potential to leach.

In the aquatic environment, fluxapyroxad is persistent, partitioning from the water column to sediments. Biotransformation of fluxapyroxad in the whole aquatic system is slow. Photolysis and hydrolysis are not important routes of transformation for fluxapyroxad in the aquatic environment.

Fluxapyroxad and its major transformation products present negligible risks to wild mammals, birds, earthworms, terrestrial plants, bees and other arthropods. Potential risks to aquatic organisms were identified from exposure to fluxapyroxad end use products. Potential risks were greater for end use products containing pyraclostrobin (BAS 703 01 F Fungicide and BAS 703 02 FFungicide). Potential risks from BAS 703 01 F Fungicide and BAS 703 02 F Fungicide to aquatic organisms are driven by the presence of pyraclostrobin and are consistent with previous PMRA assessments of this active ingredient. For all products that are used as foliar sprays, potential risks to aquatic ecosystems resulting from drift can be mitigated with no-spray buffer zones. Spray buffer zones were calculated based on toxicity endpoints for end-use products. Proposed no-spray buffer zones are considerably larger for aerial applications of BAS 703 01 F Fungicide and BAS 703 02 F Fungicide due to the inclusion of pyraclostrobin in these products.

Value Considerations

What Is the Value of BAS 700 01F Fungicide, BAS 700 04F Fungicide, BAS 703 01F Fungicide, BAS 703 02F Fungicide, BAS 700 02F Fungicide Seed Treatment and BAS 700 03F Fungicide Seed Treatment?

BAS 700 01F Fungicide and BAS 700 04F Fungicide

Fluxapyroxad, the active ingredient in BAS 700 01F Fungicide and BAS 700 04F Fungicide, controls or suppresses various fungal diseases on vegetable crops, fruit crops, cereals and oilseed crops.

BAS 700 01F Fungicide (containing 62.5 g/L fluxapyroxad) and BAS 700 04F Fungicide (containing 300 g/L fluxapyroxad) are products formulated as foliar and in-furrow treatments against various fungal diseases on many agricultural crops. Both BAS 700 01F Fungicide and BAS 700 04F Fungicide offer additional tools for disease and resistance management, and can be integrated into an overall disease management program.

BAS 703 01F Fungicide and BAS 703 02F Fungicide

Fluxapyroxad and pyraclostrobin, the active ingredients in BAS 703 01F Fungicide and BAS 703 02F Fungicide, control or suppress various fungal diseases on some oilseed crops, legumes and alfalfa, cereal grains, corn, soybean and grasses for seeds.

BAS 703 01F Fungicide (containing 250 g/L fluxapyroxad and 250 g/L pyraclostrobin) is formulated as a foliar treatment against various fungal diseases on some oilseed crops, legumes and alfalfa. BAS 703 02F Fungicide (containing 167 g/L fluxapyroxad and 333 g/L pyraclostrobin) is formulated as a foliar treatment against various fungal diseases on cereal grains, corn, soybean and forage grasses for seeds.

The combination of pyraclostrobin and fluxapyroxad provides a high level of efficacy against many diseases, and a management strategy for fungal populations that may contain isolates resistant to either compound. The combination will also increase the spectrum disease control with two modes of action.

BAS 700 02F Fungicide Seed Treatment and BAS 700 03F Fungicide Seed Treatment

Fluxapyroxad, the active ingredient in BAS 700 02F Fungicide Seed Treatment and BAS 700 03F Fungicide Seed Treatment, controls seed rot and seedling blight on soybean.

BAS 700 02F Fungicide (containing 325.5 g/L fluxapyroxad) and BAS 700 03F Fungicide (containing 333 g/L fluxapyroxad) are products formulated as seed treatments against seed rot and seedling blight on soybean. Both fungicides provide preventive seed and seedling protection against seed- and soil-borne fungal pathogens including *Rhizoctonia solani* and *Fusarium solani*.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of BAS 700 01F Fungicide, BAS 700 02 F Fungicide Seed Treatment, BAS 700 03 F Fungicide Seed Treatment, BAS 700 04 F Fungicide Seed Treatment, BAS 703 01 F Fungicide and BAS 703 02 F Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with fluxapyroxad on the skin or through inhalation of spray mists, anyone mixing/loading and applying BAS 700 01 F Fungicide or BAS 700 04 F Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and goggles or face shield. Since BAS 703 01 F Fungicide and BAS 703 02 F Fungicide are co-formulations with pyraclostrobin, mixer/loader/applicators require additional PPE: coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves and goggles or a face shield. Custom applicators treating crops with BAS 703 01 F Fungicide and BAS 703 02 F Fungicide must also use groundboom equipment with an enclosed cab. Workers treating with BAS 700 02 F Fungicide Seed Treatment or BAS 700 03 F Fungicide Seed Treatment and handling treated seed must wear the following PPE. Treaters and cleaners must wear coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks. Baggers, bag sewers, stackers, planters and other workers must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes, and socks. In addition, standard label statements to protect against drift during application were added to the labels.

Environment

Spray buffer zones for non- target aquatic habitats are required;

- 15 metres for the protection of sensitive marine ecosystem
- 1 to 450 metres, depending on the type of application equipment, for the protection of sensitive freshwater ecosystem

A statement advising that the use of fluxapyroxad may result in contamination of groundwater, particularly in areas where soils are permeable and/or the depth to the water table is shallow.

Additional advisory statements to protect non-target aquatic organisms and to advise users of the potential for fluxapyroxad residues to runoff to adjacent aquatic habitats.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2012-09, *Fluxapyroxad* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.